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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/596,419 | 06/13/2006 | Ana Maria Castano Mansanet | X-15766 | 6407 |

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| EXAMINER |
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CHANDRAKUMAR, NIZAL S

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| ART UNIT | PAPER NUMBER |
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1625

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| NOTIFICATION DATE | DELIVERY MODE |
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12/04/2007

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

Office Action Summary

Application No.

10/596,419

Applicant(s)

CASTANO MANSANET ET AL.

Examiner

Nizal S. Chandrakumar

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4,6,7,9,11,15 and 25 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-4,6,7,9,11,15 and 25 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

This application filed 06/13/2006 is a 371 of PCT/US05/00004 01/05/2005 which claims benefit of 60/552,080 03/10/2004.

Claims 1-4, 6, 7, 9, 11, 15, 25 are before the Examiner.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 1, 7, 11 and 15 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention.

In claim 1, R4, R5, R6, R7, R8 and R8 are defined but not pictured.

In claims 7, 11 and 15, it is unclear what the variable R4 is drawn to.

Claim 25 provides for the use of compounds, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 25 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6, 7, 9, 11, 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a limited class of compounds of the formula I, does not reasonably provide enablement for the plurality of general structures claimed. The specification is enabling for making many compounds wherein X = S but only one compound wherein X = O (the only other X = O compound is acid of the ester). The specification is not enabling for the plethora of compounds resulting from the laundry list of substituents layered on top of substituents. Further it is not seen where the specification discloses biological data for these compounds. As such, the specification does not enable any person skilled in the art to which it pertains, or with which is most nearly connected, to make or use the compounds of the invention commensurate in scope of these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: (1) breadth of the claims; (2) nature of the invention; (3) state of the prior art; (4) amount of direction provided by the inventor; (5) the level of predictability in the art; (6) the existence of working examples; (7) quantity of experimentation needed to make or use the invention based on the content of the disclosure; and (8) relative skill in the art.

All of the factors have been considered with regard to the claim, with the most relevant factors discussed below:

Nature of the invention: The present invention relates to thiophene and furan compounds and their pharmaceutically acceptable salts allegedly useful in the treatment of various CNS disorders.

The breadth of claims: Claimed compounds of formula I include large number of independent variables in which the substituents are layered on top of substituents leading to large number of conceivable structures.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in

the art of organic and medicinal chemistry, it is noted that each embodiment of the invention is required to be individually assessed for viability.

The amount of direction provided by the inventor and the presence or absence of working examples: The guidance and working examples provided in the specification is limited.

The direction provided in the specification is enabling for making many thiophene compounds wherein R₂ is COOH (or the corresponding ester). While some of these enabled compounds are potential precursors to other claimed compounds by functional group transformations, it is unclear how sulfonic and phosphonic acid derivatives are made. It appears that, the enolate (or its equivalent) of thioglycolate reaction product forms the crucial bond necessary for the formation of the thiophene ring system. The specification does not provide citations (commercial or literature) starting materials usable that could substitute for the lack of working examples with respect to R₂ sulfonic acid and phosphonic acid derivatives.

The specification provides one example for the formation of furan structure. Based on the possible mechanistic rationale for the formation of the furan ring in this lone example, it appears that the disclosed methods for the formation of the thiophene nucleus are not extendable for making furan compounds with all the claimed variables.

The specification does not provide any biological data for any of the compounds.

The state and the predictability of the art: With regards to making of the compounds, the state of the art is unpredictable as to functional group compatibility during many chemical transformations, in spite of major advances in protecting group strategies in synthesis. The above-mentioned unpredictabilities with regards to the applicability of methods of construction of thiophene rings to furan rings establishes that the contemporary knowledge in the art of organic synthesis would prevent one of ordinary skill in the art from accepting any claimed process described in the working examples on its face as universally applicable for making all structures encompassed by the formula I.

With regards to using of the compounds, the medicinal chemistry art is unpredictable as to which

compound would have the desired biological activity. Further, there is no disclosure in the specification with regards to the pharmacophore needed for the modulation of AMPA receptor activity.

The quantity of experimentation: In the instant case, there is a substantial gap between what is demonstrated and the breadth of the claims. Given the absence of disclosure of biological activity for any of the structures and lack of disclosure with regards to the minimum pharmacophore, in order to utilize the invention as claimed, the skilled artisan would be presented with an unpredictable amount of experimentation. The instant disclosure is broad and generic. It is unclear what specific embodiments of the compound of formula I claimed would be required in order for one of ordinary skill in the art at the time of the application, to make and use the instant invention commensurate with the scope of the claims.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claim 1 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Augustin et al. (Tetrahedron, 32(24), 3055-61, 1976).

Augustin et al. teach compounds of formula I (see Table 2, Table 3 and Table 4)

For example, compound 4a in Table 2 of Augustin et al. corresponds to compound of formula I of the instant claims wherein R1 is SCH3, R2 is CN and A is Br.

6. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Reux et al. (Sulfur Letters, 13(5), 197-202, 1991).

Reux et al. teach compounds of formula I (see Table 1)

For example compound 3e in Table 1 of Reux et al. corresponds to compound of formula I of the instant claims wherein R1 is NH₂, R2 is CN and A is OCH₃.

7. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Abdulla et al. (EP-0273602 A).

8. Abdulla et al. several compounds of formula I. For example, compound page 5, line 42-43 of Abdulla et al. corresponds to compound of formula I of the instant claims wherein R1 is SCH₃, R2 is COOH and A is C1-alkyl.

No claims are allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nizal S. Chandrakumar whose telephone number is 571-272-6202. The examiner can normally be reached on 8.30 am – 5 pm Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached at 571-272-0867 or Primary Examiner D. Margaret Seaman can be reached at 571-272-0694. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Nizal S. Chandrakumar



D. MARGARET SEAMAN
PRIMARY EXAMINER